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ORGANOPALLADIUM COMPLEXES 5-AMINO-3*H*-1,3,4-THIADIAZOLINE-2-THIONE AS METALLORECE PTOR

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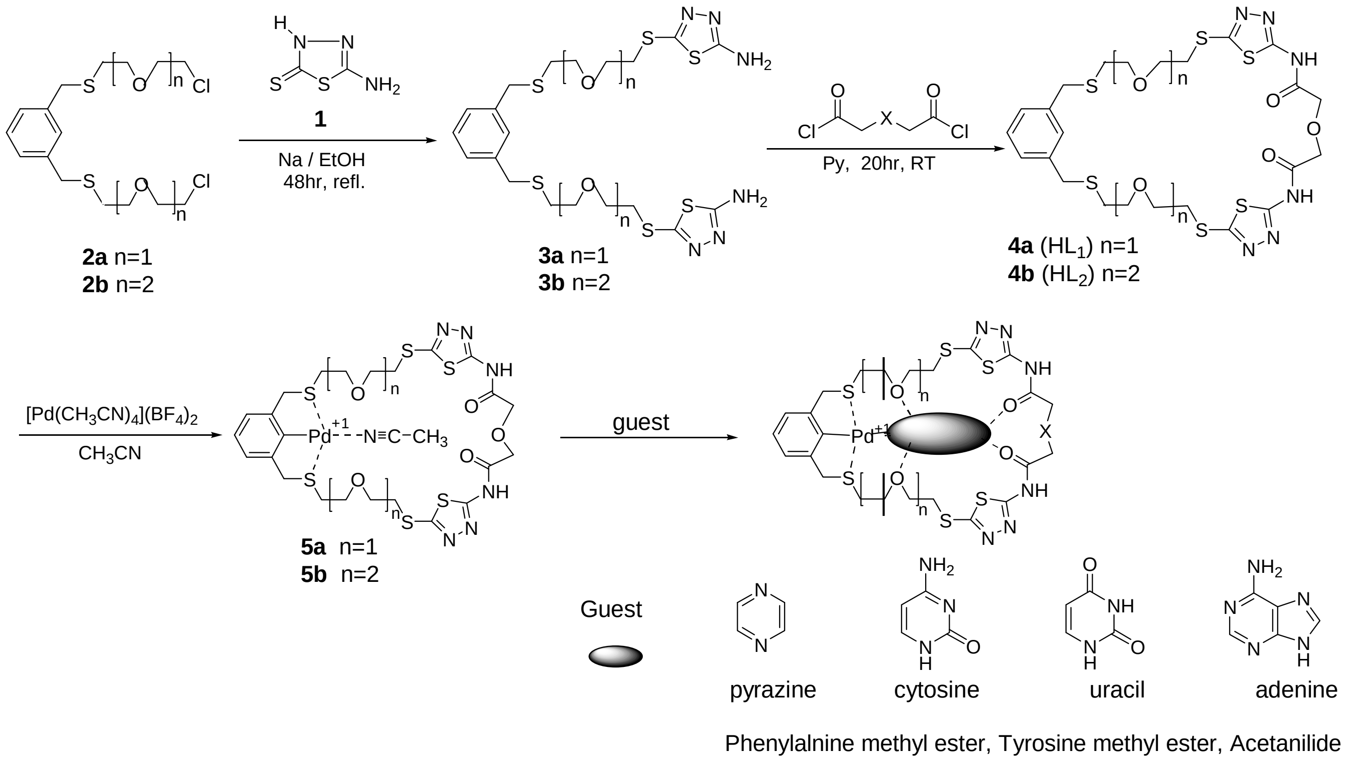
Abstract – Macrocycles containing two 5-amino-3*H*-1,3,4-thiadiazoline-2-thione 5 linking the 2- and 5-positions of the heterocycle unit and one 1,3-benzenedimethanethiol were prepared *via* the regiospecific *S*-alkylation of 5-amino-3*H*-1,3,4-thiadiazoline-2-thione. The 1,3-benzenedimethanethiol sites chelated to palladium metal ion to afford an organopalladium metalloreceptor. The structures of the macrocycles and metalloreceptors were established using ^{1}H and ^{13}C NMR, IR, MS spectrometry, and elemental analysis. The molecular recognition of the metalloreceptors (**5a** and **5b)** was examined for some DNA/RNA nucleobases and some amino acid methyl ester by ^{1}H NMR spectrometry. In case of **5a**, the complexation ability increased in the order pyrazine / uracil /acetanilide < adenine < cytosine < phenylalanine methyl ester / tyrosine methyl ester. With **5b**, the complexation ability also increased in the same order as **5a** pyrazine / uracil <acetanilide <adenine < cytosine, however, the formation constants are larger than in case of **5a**.

INTRODUCTION

Molecular recognition results from intermolecular forces acting on complementary surfaces. Metalloreceptors are transition metal complexes containing peripheral sites capable of hydrogen-bonding or π-stacking interactions, and serve as hosts for neutral guests.[1-12] Organopalladium metalloreceptors use σ-donation to a transition metal (Pd) and non-covalent second-sphere interactions, such as hydrogen bonding and π-stacking, to produce molecule recognition.[3-12] These complexes act as metalloreceptors for various substances, such as water,[4] ammonia,[4] hydrazine,[4] the hydrazinium ion,[4] pyridine,[5,6] 4-phenylpyridine,[5,6] DNA nucleobases,[7,10,11] 4,4'-bipyridine,[12] pyrazine,[12] pyrimidine,[12] *p*-aminopyridine,[11] *m*-aminopyridine[11] and *o*-aminopyridine derivatives.[8] The structures of those complexes include thiacyclophane, benzocrown ether, and calixarene. In constructing macrocycles, polydentate macrocyclic compounds containing heterocyclic ring subunits possess a variety of interesting properties, and provide hydrogen bonding sites. Therefore, we tried to prepare organopalladium metalloreceptors containing heterocyclic compounds, such as two 5-amino-3*H*-1,3,4-thiadiazoline-2-thione and 1,3-benzenedimethanethiol as subunits. Here, we report the synthesis of metalloreceptors along with studies of the molecular recognition of the nucleic acid bases, cytosine, adenine, uracil, pyrazine, acetanilide, phenylalanine methyl ester and tyrosine methyl ester.

RESULTS AND DISCUSSION

The tautomeric behavior of 5-amino-3*H*-1,3,4-thiadiazoline-2-thione (**1**)[13] and its regiospecific *S*-alkylation[14] under basic conditions have been reported. Utilizing these reactions, macrocycles containing two 2-amino-5-alkylthio-1,3,4-thiadiazole and 1,3-benzenedimethanethiol subunits were prepared from **1**, as shown in Scheme 1.



Scheme 1. Synthesis of macrocycles and palladium metalloreceptors.

As *α*,*α*'-*m*-xylenedithiol is a palladation chelation site,[3-9, 15-18] an *α*,*α*'-*m*-xylenedithiol moiety was introduced to macrocyclic compounds to chelate palladium. According the regiospecific *S*-alkylation of **1**, the reaction of **1** with either *α,α*'-bis(5-chloro-3-oxapentylthio)-*m*-xylene (**2a**) or *α,α*'-bis(8-chloro-3,5-dioxaoctylthio)-*m*-xylene (**2b**) in the presence of NaOEt in ethanol gave an (*S*)-alkylated dimer (**3**). The difference between **2a** and **2b** is the length of the chain, which influences the size of the macrocycle cavity. The formation of **3** was confirmed by ^{1}H and ^{13}C NMR spectra. In **3a**, the NH of compound (**1**) was replaced by SCH_2 signals at 3.23 and 33.8 ppm in the ^{1}H and ^{13}C NMR spectra, respectively. In the ^{13}C NMR, the thione part of **1** (181.0 ppm) typically changed to the thio group of **3a** (169.5 ppm). To obtain target macrocycles containing two 2-amino-5-alkylthio-1,3,4-thiadiazole and one 1,3-benzenedimethanethiol from **3**, we attempted Cs^+-mediated[19, 20] cyclization involving *N,N'*-diacylation of **3** at the NH_2 of the 1,3,4-thiadiazole rings using diglycolyl chloride with a high-dilution technique. Diglycolyl chloride was added to a CH_2Cl_2 solution of **3** over a 20 hr period. The structure of the macrocycle was established using ^{1}H and ^{13}C NMR, IR, and FAB-HRMS. The successful macrocyclization of **3a** to **4a** was supported by evidence of *N*-acylation, which indicated that an $NHCOCH_2O$ group replaced the NH_2 at 12.57 and 4.47 ppm in the ^{1}H spectrum and at 159.7 and 74.1 ppm in the ^{13}C NMR spectrum. The IR spectrum also showed the carbonyl group of the amide at 1686 cm^{-1}. FAB-HRMS clearly supported structure (**4a)** (675.0683).

Macrocycles (HL), including an *m*-thiacyclophane moiety, can be palladated to produce organopalladium complexes that contain an open coordination site on palladium *trans* to the Pd-C bond.[3-10, 15-18] The synthesized macrocyclic compounds (**4a**-**4b**) were easily palladated by refluxing an acetonitrile solution of the ligand (HL) in the presence of 1 equivalent of $[Pd(CH_3CN)_4][BF_4]_2$. Metalloreceptors were prepared by replacing the labile acetonitrile ligand with 1 equivalent of the substrate molecule. All the spectroscopic and analytical data were consistent with palladation and the formula $[Pd(L)(CH_3CN)][BF_4]]$. In case of **5a**, the resonances of the benzylic CH_2S protons were shifted downfield (4.52 ppm) and were broad in the ^{1}H NMR spectrum compared with those of the free ligand HL (3.74 ppm). The aromatic four hydrogens were substituted to three hydrogens. And one equivalent of CH_3CN was observed in ^{1}H NMR. These results are very similar to that previously reported.[10] The effect of palladation was also evident in the ^{13}C NMR spectrum, with the resonance of the resonance of benzylic carbon atoms shifted downfield by 8.1 ppm (from 36.8 ppm to 44.9 ppm).[10] And the resonance of carbon atom bonded to Pd shifted at 155.4 ppm from 129.7 ppm. A strong ion peaks for $[Pd(L)]^+$ in the FAB-HR mass spectrum (778.9562) were strongly supported by evidence of formation of palladation. The resulting complexes were colorless, air-stable solid that were soluble in most polar organic solvents.

Metalloreceptors can coordinate a substrate molecule by σ-donation to the Pd center while simultaneously interacting with the peripheral oxygen and nitrogen atoms of the thiadiazoline rings and the side chains *via* hydrogen bonding. To examine the molecular recognition (coordination) of the synthesized metalloreceptors, the ^{1}H NMR spectrum were checked in the presence of a guest molecule, such as cytosine, adenine, uracil, pyrazine, acetanilide, phenylalanine methyl ester and tyrosine methyl ester. Host molecule was dissolved in DMSO-d_6 (0.01-0.02 M) and the guest stock solutions in DMSO-d_6 (0.04 - 0.08 M) were added several times with small increments until the ^{1}H NMR chemical changes have been stopped. ^{1}H NMR spectra were recorded at each addition and the calculated complexation constants are listed in Table 1. Uracil, pyrazine and acetanilide did not produce any change in the ^{1}H NMR chemical shift of **5a** upon addition of up to ten equivalents, which means there is no interaction between **5a**. Uracil and pyrazine similarly did not produce any change in the ^{1}H NMR chemical shift of **5b**. By contrast, significant ^{1}H NMR chemical shifts of **5a** were seen with phenylalanine methyl ester and tyrosine methyl ester additions. One equivalent of guest molecule was sufficient to produce a complete change of chemical shift, therefore, the estimated complexation constants (K) were larger than 10^4 (K = [HG]/[H][G]), where, H = host, G = guest, and HG = host-guest complex).

Table 1. The calculated complexation constants (K)[a] with the chemical shift changes (Δ**δ**) of $ArCH_2S$ in metalloreceptor (**5**) upon the addition of guest molecules.

Guest		Cytosine	Adenine	Uracil	Pyrazine	acetanilide	Phenyl-alanine methyl ester	Tyrosine methyl ester
Host **5a**	K (M^{-1})	2.16±0.24 x 10^3	7.56 ±0.53 x 10^2	<1 [b,d]	<1 [b,d]	<1 [b,d]	>1 x 10^4 [c,d]	>1 x 10^4 [c,d]
Host **5b**	K (M^{-1})	>1 x 10^4 [c,d]	1.19 ±0.10 x 10^3	<1 [b,d]	<1 [b,d]	1.86 ±0.14 x 10^2	-	-

[a] K was obtained from the slope of the plot ([HG]/[H] vs [G]) in the ^{1}H NMR titration experiment.
[b] No chemical shift changes upon the addition of up to ten equivalents of guest molecules.
[c] One equivalent of guest molecule was sufficient to produce a complete change of chemical shift.
[d] These values were estimated from the approximation that peaks less than 1/10 of major peak intensity usually can not be recognized by NMR technique. Thus, K = (0.001M)/(0.01M x 0.1 M) = 1 M^{-1} and K = (0.01M)/(0.001M)(0.001M) = 10000M^{-1} under experimental conditions.

The complexation ability of **5a** increased in the order pyrazine / uracil /acetanilide < adenine < cytosine < phenylalanine methyl ester / tyrosine methyl ester. In case of **5b**, the complexation ability also increased in the same trend as **5a** pyrazine / uracil <acetanilide <adenine < cytosine and the formation constants are larger than in case of **5a**. The difference between **5a** and **5b** is the length of the chain between thiadizoline ring and *m*-xylenedithiol, which influences the size of the macrocycle cavity.

Even though the perfect explanation for the results in Table 1 is not simple, it is clear that the basicity of the guest is the most important factor in making complexes. Since aliphatic amines are more basic than aromatic amines, amino acid methyl esters have the largest complexation constants. In the nucleic acid bases, there are many possible binding sites, but it has been found that metal ion binding occurs predominantly at N3 in pyrimidine bases, and at N1 or N7 in purine bases, respectively.[21] The basicity at N3 in cytosine and N1 in adenine is much higher than that at any nitrogen sites in pyrazine / uracil /acetanilide. The difference of basicity between N3 in cytosine (pK_a = 4.5) and N1 in adenine (pK_a = 4.1)[19] tells us the binding ability of cytosine is about 2.5 (= $10^{4.5-4.1}$) times greater than that of adenine if the basicity is the only factor in complexation. The experimental values for the ratio of K(cytosine)/K(adenine) are 2.9 and larger than 8 for **5a** and **5b**, respectively. Therefore, other effects such as hydrogen bonds play an important role in stabilizing the host-guest complex. Especially, this is more important in more flexible host **(5b)**, where the conformation for hydrogen bond is much more feasible. In addition, the binding constant of **5a** (756) toward adenine is much smaller than that (6000) of the previously reported metalloreceptor (**5**)[10] which is containing two 5-amino-3*H*-1,3,4- thiadiazolin-2- ones. Even though two metalloreceptors has a big difference in binding constants, the structural difference between two metalloreceptors is connected with only a carbonyl group in heterocycle. The compound with a carbonyl group shows a large binding constant. It is due to the formation of hydrogen bonds which play an important role in stabilizing the host-guest complex.

EXPERIMENTAL

All melting points were determined on an electrically heated Thomas-Hoover capillary melting point apparatus and were uncorrected. The IR spectra were recorded on a Jasco Report-100 spectrophotometer. The ^{1}H and ^{13}C NMR spectra were obtained using a JEOL JNM-AL400 spectrometer at 400 MHz and 100 MHz respectively with tetramethylsilane as the internal reference. NMR measurements were performed at the Central Research Facilities of Chungnam National University. Elemental analyses were carried out on an EA 1110 (CE Instrument). FAB-HRMS spectra were obtained on a JEOL-JMS HX-100/110A spectrometer at Korea Basic Science Institute, Taeduk, Taejon.

Syntheses of 5-amino-3*H*-1,3,4-thiadiazoline-2-thione **(1),**[13] 5-chloro-3-oxapentyl methanesulfonate[22] and α,α'-bis (5-chloro-3-oxa-pentylthio)-*m*-xylene (**2a**)[22] followed the previous procedures.

8-Chloro-3,6-dioxaoctyl methanesulfonate

The synthesis of 8-chloro-3,6-dioxaoctyl methanesulfonate followed the same procedure of the preparation of 5-chloro-3-oxapentyl methanesulfonate.[22] Colorless liquid, yield (98%). R_f: 0.38 (*n*-hexane : ethyl acetate = 1 : 1). IR (KBr pellet, cm^{-1}): 2873 (CH), 1455 (S=O). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.38 (2H, t, *J* = 5.2 Hz, CH_2OSO_2), 3.79-3.68 (8H, m, $2CH_2OCH_2CH_2OCH_2$), 3.64 (2H, t, *J* = 5.2 Hz, $ClCH_2$), 3.08 (3H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 71.1 (CH_2OSO_2), 70.4, 70.3, 69.1, 68.8 ($2CH_2OCH_2$), 42.7 (CH_2Cl), 37.5 (CH_3). Anal. Calcd for $C_7H_{15}O_5ClS$: C 34.08; H 6.13; S 13.00. Found: C 34.10; H 6.11; S 12.98.

α,α'-Bis(8-chloro-3,5-dioxaoctylthio)-*m*-xylene (2b)

The synthesis of (**2b**) followed the same procedure of the preparation of α,α'-bis(5-chloro-3-oxapentylthiol)-*m*-xylene (**2a**).[22] Liquid, yield (70%). R_f: 0.43 (*n*-hexane : ethyl acetate = 4 : 1). IR (KBr pellet, cm^{-1}): 2864 (CH), 1604 (C=C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.18 (4H, m, C_6H_4), 3.76 (4H, s, $2C_6H_4C\underline{H}_2S$), 3.72-3.69 (4H, m, $2CH_2Cl$), 3.67-3.66 (4H, m, $2OC\underline{H}_2CH_2Cl$), 3.56-3.49 (12H, m, $2CH_2OCH_2CH_2O$), 2.55 (4H, t, 6.60 Hz, $2C_6H_4CH_2SC\underline{H}_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.8, 129.3, 128.3, 127.4 (C_6H_4), 70.5, 70.0, 69.7, 69.5 ($2CH_2OCH_2$), 43.6 (CH_2Cl), 35.3 ($C_6H_4\underline{C}H_2S$), 30.1 ($C_6H_4CH_2S\underline{C}H_2$). Anal. Calcd for $C_{20}H_{32}O_4Cl_2S_2$: C 50.95; H 6.84; S 13.60. Found: C 50.97; H 6.85; S 13.58.

α,α'-Bis[5-(5-amino-1,3,4-thiadiazol-2-yl)thio]-3-oxapentylthio]-*m*-xylene (3a)

5-Amino-3*H*-1,3,4-thiadiazoline-2-thione **(1)** (7.3 g, 54.8 mmol) was dissolved in EtOH-(350 mL)-Na (1.44 g, 62.6 mmol) solution. α,α'-Bis (5-chloro-3-oxapentylthio)-*m*-xylene **(2a)** (10.0 g, 26.1 mmol) was added to the above solution and the reaction mixture was stirred at reflux for 48h. Solvent was removed under reduced pressure and the residue was dissolved in THF. The undissolved 5-amino-3*H*-1,3,4-thiadiazoline-2-thione and salt were filtered off. The THF was distilled off under reduced pressure, and the residue was column chromatographed using *n*-hexane : EA : ethanol (3 : 3 : 2) as eluent affording yellow solid product (7.7 g, 51.0%). mp: 72-73 °C. R_f: 0.17 (*n*-hexane : EA = 1 : 5). IR (KBr pellet, cm^{-1}): 3299 (NH), 2994 (CH), 1629 (C=N). ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.23 (4H, br, $2NH_2$), 7.28-7.18 (4H, m, C_6H_4), 3.76 (4H, s, $2C_6H_4\ C\underline{H}_2SCH_2$), 3.62 (4H, t, J = 6.2 Hz, $2OC\underline{H}_2CH_2SHet$), 3.53 (4H, t, J = 6.6 Hz, $2C_6H_4CH_2SCH_2C\underline{H}_2O$), 3.23 (4H, t, J = 6.2 Hz, $2CH_2CH_2OCH_2C\underline{H}_2SHet$), 2.54 (4H, t, J = 6.6 Hz, $2C_6H_4CH_2SC\underline{H}_2$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.5 (S-C=N), 150.1 (N-C=N), 138.8, 129.4, 128.4, 127.5 (C_6H_4), 69.9, 68.6 ($\underline{C}H_2O\underline{C}H_2$), 35.3 ($C_6H_4\underline{C}H_2S$), 33.8 ($CH_2SHet$), 30.0 ($C_6H_4CH_2S\underline{C}H_2$). Anal. Calcd for $C_{20}H_{28}N_6O_2S_6$: C 41.64; H 4.89; N 14.57. Found: C 41.65; H 4.87; N 14.55. MS (EI) (*m/z*, relative intensity): 576 (M^+), 372, 357, 236, 178, 160, 147, 133, 105, 91, 77, 59.

α,α'-Bis[8-(5-amino-1,3,4-thiadiazol-2-yl)-3,6-dioxaoctylthio]-*m*-xylene (3b)

The synthesis of **3b** followed the same procedure of the preparation of **3a** except chromatography eluent ($CHCl_3$: MeOH = 20 : 1). Yield 57.6%, mp: 59-60 °C. R_f: 0.40 ($CHCl_3$: MeOH = 9 : 1). IR (KBr pellet, cm^{-1}): 3103 (NH), 2866 (CH), 1631 (C=N). ^{1}H NMR (400 MHz, $CDCl_3$: CD_3CN = 1 : 1): δ 7.28-7.17 (4H, m, C_6H_4), 5.99 (4H, br, $2NH_2$), 3.75 (4H, s, $2C_6H_4C\underline{H}_2S$), 3.73 (4H, t, J = 6.2 Hz, $2OC\underline{H}_2CH_2SHet$), 3.59-3.54 (12H, m, $2OC\underline{H}_2C\underline{H}_2OC\underline{H}_2CH_2\ SHet$), 3.20 (4H, t, J = 6.2 Hz, $C\underline{H}_2SHet$), 2.55 (4H, t, J = 6.6 Hz, $2C_6H_4CH_2SC\underline{H}_2$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.1 (S-C=N), 154.5 (N-C=N), 140.6, 131.1, 130.2, 129.2 (C_6H_4), 72.3, 71.9, 71.6, 71.0 ($CH_2OCH_2CH_2OCH_2$), 37.8 ($C_6H_4\underline{C}H_2S$), 35.9 (CH_2SHet), 32.2 ($C_6H_4CH_2S\underline{C}H_2$). Anal. Calcd for $C_{24}H_{36}N_6O_4S_6$: C 43.35; H 5.46; N 12.64; S 28.93. Found: C 43.37; H 5.46; N 12.65; S 28.94. MS (EI) (*m/z*, relative intensity): 664 (M^+), 416, 280, 222, 177, 160, 133, 105, 60.

11,12,14,20,22,23-Hexaaza-6,17,28-trioxa-3,9,25,31,38,39-hexathiotetracyclo[31,3,1,1^{10,13},1^{21,24}]nonatriaconta-1(37),10(11),12 (13),21(22),23(24),33(34),35(36)-heptaene-15,19-dione (4a)

α,α'-Bis[5-(5-amino-1,3,4-thiadiazol-2-yl)thio]-3-oxapentylthio]-*m*-xylene **(3a)** (2.28 g, 3.95 mmol) was dissolved in dichloromethane (450 mL)-pyridine (0.64 mL, 7.90 mmol) and cesium chloride (0.20 g, 1.21 mmol) was added. Diglycoly chloride (1.01 g, 5.92 mmol)-dichloromethane (50.0 mL) solution was added to the above solution for 20 h. After completion of reaction, the reaction mixture was washed with 1*N* HCl (100 ml), organic layer was dried with $MgSO_4$. Solvent was removed under reduced pressure and then the residue was column chromatographed using *n*-hexane : EA (1 : 9) as eluent affording colorless solid product (0.51 g 19.1%). mp: 162-163 °C. R_f: 0.30 (*n*-hexane : ethyl acetate = 1 : 9). IR (KBr pellet, cm^{-1}): 3167 (NH), 2916 (CH), 1686 (C=O), 1533 (C=N). ^1H NMR (400 MHz, $CDCl_3$): δ 12.57 (2H, br, 2NH), 7.27-7.18 (4H, m, C_6H_4), 4.47 (4H, s, $2COC\underline{H}_2O$), 3.75 (4H, t, *J* = 6.7 Hz, $2C_6H_4CH_2SCH_2C\underline{H}_2O$), 3.74 (4H, s, $2C_6H_4C\underline{H}_2S$), 3.60 (4H, t, *J* = 6.4 Hz, $2OC\underline{H}_2CH_2SHet$), 3.41 (4H, t, *J* = 6.4 Hz, $2OCH_2C\underline{H}_2SHet$), 2.61 (4H, t, *J* = 6.7 Hz, $2C_6H_4CH_2SC\underline{H}_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7 (S-C=N), 159.7 (C=O), 157.5 (N-C=N), 138.8, 129.7, 129.0, 127.9 (C_6H_4), 74.1 (O=C-$\underline{C}H_2$), 70.8, 69.3 (CH_2OCH_2), 36.8 ($C_6H_4\underline{C}H_2S$), 33.0 (CH_2SHet), 31.0 ($C_6H_4CH_2S\underline{C}H_2$). FABHRMS calcd for $C_{24}H_{31}N_6O_5S_6$ 675.0680, found 675.0683.

14,15,17,23,25,26-Hexaaza-6,9,20,31,34-pentaoxa-3,12,28,37,44,45-hexathiotetracyclo[37,3,1,1^{13,16},1^{24,27}]pentatetraconta-1(43),13(14),15(16),24(25),26(27),39(40),41 (42)- heptaene-18,22-dione (4b)

The synthesis of **4b** followed the same procedure of the preparation of **4a**. Yield 75.2%, mp: 89℃. R_f: 0.20 (*n*-hexane : ethyl acetate = 1 : 9). IR (KBr pellet, cm^{-1}): 3167 (NH), 2916 (CH), 1686 (C=O), 1533 (C=N). ^1H NMR (400 MHz, DMSO-d_6): δ 12.66 (2H, br, 2NH), 7.20-7.12 (4H, m, C_6H_4), 4.43 (4H, s, $2COC\underline{H}_2O$), 3.73 (4H, t, *J* = 5.6 Hz, $2OC\underline{H}_2CH_2SHet$), 3.71 (4H, s, $2C_6H_4C\underline{H}_2S$), 3.54-3.45 (12H, m, $2CH_2OCH_2CH_2O$), 3.40 (4H, t, *J* = 5.6 Hz, $2OCH_2C\underline{H}_2SHet$), 2.49 (4H, t, *J* = 5.4 Hz, $2C_6H_4CH_2SC\underline{H}_2$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.5 (S-C=N), 159.3 (C=O), 158.4 (N-C=N), 138.8, 129.2, 128.3, 127.4 (C_6H_4), 70.1 (O=C-$\underline{C}H_2$), 69.8, 69.7, 69.7, 69.2 (CH_2OCH_2), 35.4 ($C_6H_4\underline{C}H_2S$), 33.5 (CH_2SHet), 30.2 ($C_6H_4CH_2S\underline{C}H_2$). FAB-HRMS calcd for $C_{28}H_{39}N_6O_7S_6$ 763.1205, found 763.1202.

Metalloreceptor [Pd(L_1)(CH_3CN)(BF_4)] (5a)

Macrocyle **(4a)** (0.40 g, 0.59 mmol) was dissolved in CH_3CN (160 ml) and $[Pd(CH_3CN)_4](BF_4)_2$ (0.26 g, 0.59 mmol) in CH_3CN (20.0 ml) solution was added to the above solution. The reaction mixture was stirred at reflux for 2 h. After the completion of reaction, solvent was removed under reduced pressure, CH_3CN (3mL) solution was kept in ice box for recrystallization to afford colorless solid product (79.3 mg, 16.3%). mp: 189 °C. R_f: 0.13 ($CHCl_3$: MeOH = 9 : 1). IR (KBr pellet, cm^{-1}): 3433(NH), 2995 (CH), 1681 (C=O), 1540 (C=N), 1076 (Pd-C). ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.01 (2H, br, 2NH), 7.02 (3H, m, C_6H_3), 4.52 (8H, br, $2COC\underline{H}_2O$ + $C_6H_3C\underline{H}_2S$), 3.75-3.68 (8H, br, $2OCH_2CH_2O$), 3.33 (4H, br, $CH_2C\underline{H}_2SHet$), 3.19 (4H, br, $C_6H_3CH_2SC\underline{H}_2$), 2.06 (3H, s, $C\underline{H}_3CN$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.4 (S-C=N), 159.0 (C=O), 156.1 (N-C=N), 155.4, 150.3, 125.4, 122.6 (C_6H_3), 118.0 ($CH_3\underline{C}N$), 71.5 ($CO\underline{C}H_2O$), 69.7, 68.1 ($\underline{C}H_2O\underline{C}H_2$), 44.9 ($C_6H_3\underline{C}H_2S$), 38.6 ($\underline{C}H_2SHet$), 33.4 ($C_6H_3CH_2S\underline{C}H_2$), 1.2 ($\underline{C}H_3CN$). FAB-HRMAS calcd for $C_{24}H_{29}N_6O_5S_6Pd^+$(-$CH_3CN$), 778.9565, found : 778.9562.

Metalloreceptor [Pd(L_2)(CH_3CN)(BF_4)] (5b)

The synthesis of **5b** followed the same procedure of **5a**. Yield 25.2%, mp: 165℃. R_f: 0.16 ($CHCl_3$: MeOH = 20 : 1). IR (KBr pellet, cm^{-1}): 3175 (NH), 2993 (CH), 1694 (C=O), 1539 (C=N), 1083 (Pd-C). ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.78 (2H, br, 2NH), 7.00 (3H, br, C_6H_4), 4.51 (8H, br, $2COC\underline{H}_2O$ + $2C_6H_3C\underline{H}_2$), 3.75- 3.51 (16H, br, $2CH_2OCH_2CH_2OCH_2$), 3.44 (4H, br, $2CH_2C\underline{H}_2SHet$), 3.25 (4H, br, $2C_6H_3CH_2SC\underline{H}_2$), 2.08 (3H, s, $C\underline{H}_3CN$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.2 (S-C=N), 159.9 (C=O), 156.7 (N-C=N), 159.0, 150.8, 126.0, 123.4 (C_6H_3), 118.8 ($CH_3\underline{C}N$), 72.6 ($O\underline{C}H_2C$=O), 71.1, 70.4, 70.1, 69.1 ($2\underline{C}H_2O\underline{C}H_2$), 45.9 ($C_6H_3\underline{C}H_2S$), 39.1 ($CH_2SHet$), 35.4 ($C_6H_3CH_2S\underline{C}H_2$), 1.3 ($\underline{C}H_3CN$). FAB-HRMS calcd for $C_{28}H_{37}N_6O_7S_6Pd^+$ (-CH_3CN) 867.0083, found 867.0081.

Molecular recognition of metalloreceptors (5)

The solution of host molecule (0.01-0.02 M) was prepared in DMSO-d_6 and the guest stock solutions in DMSO-d_6 (0.04-0.08 M) were added several times small increments until ^{1}HNMR chemical shifts have been stopped.. ^{1}H NMR of the host molecules were measured in presence of the guest molecules.

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